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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/462,61[illegible]	[illegible]	L[illegible]	X [illegible]038-1003-MI[illegible]

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EXAMINER	
WHITEMAN, B	
ART UNIT	**PAPER NUMBER**
1633	9

DATE MAILED: 08/02/01

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

PTO-90C (Rev.11/00)

1- File Copy

Office Action Summary	Application No.	Applicant(s)	
	09/462,816	LI ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1633	

-- The MAILING DATE of this communication appears on the cov r sh et with the correspond nce address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *22 June 2001* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-48* is/are pending in the application.

4a) Of the above claim(s) *43-48* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-42* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Priority

This application discloses and claims only subject matter disclosed in prior Application No. 08/896,442, filed 18 July 1997, and names an inventor or inventors named in the prior application. Accordingly, this application may constitute a continuation or division. Should applicant desire to obtain the benefit of the filing date of the prior application, attention is directed to 35 U.S.C. 120 and 37 CFR 1.78.

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 120 as follows:

> An application in which the benefits of an earlier application are desired must be co-pending with the prior application or with an application similarly entitled to the benefit of the filing date of the prior application.
>
> An application in which the benefits of an earlier application are desired must contain a specific reference to the prior application(s) in the first sentence of the specification (37 CFR 1.78).

This application is a 371 of PCT/CA98/00697 filed on 16 July 1998 is acknowledged.

Information Disclosure Statement

The information disclosure statement filed on 2 February 2000 does not fully comply with the requirements of 37 CFR 1.98 because: applicant does not properly cite the journal article(s) listed on the 1449. The title of each journal article is missing.

References have been considered by the examiner, but in order to have the journal articles initialed and dated on the 1449, a new 1449 properly citing the journal articles must be filed with the response to this office action. Failure to comply with this notice will result in the above mentioned information disclosure statement being placed in the application file with the non-complying information **not** being considered. See 37 CFR 1.97(i).

Applicant elects to prosecute claims 1-42 without traverse in paper nos.7 is acknowledged.

Claims 43-48 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention, there being no allowable generic or linking claim. Election was made without traverse in Paper No. 7.

Claims 1-42, to which the following grounds of rejection are applicable, are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-29, 40-42, as best understood, are readable on a genus of an immunogenic composition comprising a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or fragment thereof, a promoter sequence operatively linked to said first nucleotide sequence; and a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein, wherein the genus of the immunogenic composition is not claimed in a specific biochemical or molecular structures that could be envisioned by one skilled in the art at the time the invention was made are rejected

under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention.

Claims 36-38, as best understood, are readable on a genus of an immunoprotection enhancing sequence to produce an enhanced immunoprotection to said RSV G protein in said host, wherein the genus of the immunoprotection enhancing sequence is not claimed in a specific biochemical or molecular structures that could be envisioned by one skilled in the art at the time the invention was made are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time of the application was filed, had possession of the claimed invention.

The specification contemplates production of a genus of the immunogenic composition described above. The specification provides sufficient description of a species of an immunogenic composition comprising a nucleotide sequence encoding a RSV G protein or a RSV G protein fragment, a promoter sequence operatively linked to said first nucleotide sequence and a second nucleotide sequence located encoding the human cytomegalovirus Intron A between said first nucleotide sequence and said promoter. However, the specification does not provide sufficient description of a genus of the immunogenic composition comprising a nucleotide sequence encoding a RSV G protein or a RSV G protein fragment, a promoter sequence operatively linked to said first nucleotide sequence and a **second nucleotide sequence** located between said first nucleotide sequence and said promoter.

Furthermore, the specification contemplates production of a genus of the immunoprotection enhancing sequence to produce an enhanced immunoprotection to said RSV G protein in said host. The specification provides sufficient description of a species of an immunoprotection enhancing sequence encoding the human cytomegalovirus Intron A between said first nucleotide sequence and said promoter. However, the specification does not provide sufficient description of a genus of an immunoprotection enhancing sequence to produce an enhanced immunoprotection to said RSV G protein in said host.

It is not apparent that on the basis of applicant's disclosure, an adequate written description of the invention defined by the claims requires more than a mere statement that it is part of the invention and reference to potential methods and/or molecular structures of molecules that are essential for the genus of an immunogenic composition comprising a nucleotide sequence encoding a RSV G protein or a RSV G protein fragment, a promoter sequence operatively linked to said first nucleotide sequence and **a second nucleotide sequence located between said first nucleotide sequence and said promoter** or a genus of an immunoprotection enhancing sequence to produce an enhanced immunoprotection to said RSV G protein in said host; what is required is the knowledge in the prior art and/or description as to the availability of a representative number of species of biochemical or molecular structure of an immunogenic composition comprising a nucleotide sequence encoding a RSV G protein or a RSV G protein fragment, a promoter sequence operatively linked to said first nucleotide sequence and a second nucleotide sequence located between said first nucleotide sequence and said promoter or an immunoprotection enhancing sequence that must exhibit the disclosed biological functions as contemplated by the claims.

It is not sufficient to support the present claimed invention directed to a genus of an immunogenic composition comprising a nucleotide sequence encoding a RSV G protein or any RSV G protein fragment thereof, a promoter sequence operatively linked to said first nucleotide sequence and a second nucleotide sequence located between said first nucleotide sequence and said promoter. In addition it is not sufficient to support the present claimed invention directed to a genus of an immunoprotection enhancing sequence. The claimed invention as a whole is not adequately described if the claims require essential or critical elements, which are not adequately described in the specification and which is not conventional in the art as of applicant's effective filing date. Claiming a genus of an unspecified second nucleotide sequence, and/or a genus of an unspecified immunoprotection enhancing sequence that must possess the biological properties as contemplated by applicant's disclosure without defining what means will do so is not in compliance with the written description requirement. Rather, it is an attempt to preempt the future before it has arrived. (See *Fiers v. Revel*, 25 USPQ2d 1601 (CA FC 1993) and *Regents of the Univ. Calif. v. Eli Lilly & Co.*, 43 USPQ2d 1398 (CA FC, 1997)). Possession may be shown by actual reduction to practice, clear depiction of the invention in a detailed drawing, or by describing the invention with sufficient relevant identifying characteristics such that a person skilled in the art would recognize that the inventor had possession of the claimed invention. Pfaff v. Wells Electronics, Inc., 48 USPQ2d 1641, 1646 (1998). The skilled artisan cannot envision the detailed structure of a genus of claimed immunogenic composition described above and/or an immunoprotection enhancing sequence described above that must exhibit the contemplated biological functions, and therefore, conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the structures and/or methods disclosed in

the as-filed specification. Thus, in view of the reasons set forth above, one skilled in the art at the time the invention was made would not have recognized that applicant was in possession of the claimed invention as presently claimed.

Claims 1-42 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for 1) An immunogenic composition comprising a vector that will not replicate, wherein the vector comprises: a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment, a CMV promoter sequence operatively linked to said first nucleotide sequence for expression of said RSV G protein, a second nucleotide sequence encoding the human cytomegalovirus Intron A; 2) A method of stimulating an immune response in a mammal using an effective amount of the composition of 1; 3) A method comprising isolating gene encoding a RSV G protein or a RSV G fragment, operatively linked said gene to at least one control sequence to produce a vector that will not replicate in mammal; 4) Administering composition of 3 to a mammal, so as to stimulate an immune response in said mammal. The specification does not reasonably provide enablement for any other embodiment as encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the

invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

With respect to any claims encompassing the use of an immunogenic composition or an immunoprotection enhancing sequence of the claimed invention, the immunogenic composition or immunoprotection enhancing sequence is not supported by a sufficient written description (for possession of a genus of a genus of an immunogenic composition comprising a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or fragment thereof, a promoter sequence operatively linked to said first nucleotide sequence; and a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein and/or a genus of an immunoprotection enhancing sequence), particularly in view of the reasons set forth above, one skilled in the art would not have known how to make and/or use the claimed invention so that it would operate as intended, *e.g.* generate protective antibodies in a host and/or to produce an enhanced immunoprotection to said RSV G protein in said host.

Claims 1-42 encompasses an immunogenic composition comprising a replicant defective vector comprising a first nucleotide sequence encoding a RSV G protein or fragment thereof and a control sequence directing expression of said RSV G protein when introduced into host to produce an immune response to said RSV G protein; and operatively linking said first nucleotide sequence to a second nucleotide sequence to increase expression of said RSV G protein in vivo from the vector in the host, and a method of producing a vaccine for protection (encompasses partial/complete protection) or prevention (total protection) of a host against a disease caused by infection with RSV, including infection by a pathogen (e.g. viruses, bacteria, fungus, etc.).

Furthermore, the claimed invention includes a method of immunizing a host against disease caused by infection with RSV by using the immunogenic composition described above, wherein said a balance Th1/Th2 immune response. The invention lies in the field of producing an immunogenic composition or vaccine using a replicant defective vector encoding a viral protein (RSV G protein).

The state of the art exemplified by Gurunathan et al. indicates that the goal of developing effective vaccines for a particular disease depends on several factors:

1) Identification of a conserved antigen capable of inducing protection is an outbred population.

2) Design vaccines that can induce an appropriate qualitative and quantitative immune response.

3) Some diseases require different types of immune responses for effective primary and memory immunity (*J Immunol*, Vol. 161(9), pg. 4563, November 1998).

In addition, major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered

2) The route and time course of administration, the sites of administration, the trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

3) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method (Anderson et al., *Nature*, Vol. 392, pp. 25-30, April 1998).

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the subject being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson indicates that the state of the art before 1998, and teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30).

Anderson further teaches that the reason for the low efficiency of gene transfer and expression in a subject is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma et al., *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Thus, in view of the state of the art, producing an immunogenic composition or vaccine using a replicant defective vector encoding a nucleotide sequence is considered unpredictable.

The application provides sufficient guidance and/or factual evidence showing 1) immunization of BALB/c mice with live RSV intranasally resulted in a balance cytokine profile; 2) immunization in BALB/c mice with PXL5 or PXL6 (vectors encoding a gene encoding a full length membrane attached form of the RSV G protein and containing the CMV intron A sequence or gene encoding a secreted form of the RSV G protein lacking the trans-membrane

domain and the CMV intron A sequence as well as a nucleotide sequence encoding a signal peptide of the human tissue plasminogen activator, respectively) via either the i.m. or intradermal (i.d.) route, which gave rise to a balanced cytokine profile (page 30, lines 5-35).

However, the as-filed specification does not provide sufficient guidance and/or factual evidence demonstrating a reasonable correlation between the disclosure including its exemplified examples and the subject matter being sought in the claims wherein an immunogenic composition comprising a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment, a promoter sequence operatively coupled to said first nucleotide sequence for expression of said RSV G protein in the host, and a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein in vivo from said vector in host can be used to stimulate a vaccine effect (e.g. encompassing treatment or prevention); against any diseased or infectious antigen, particularly given all of the reasons set forth above. In addition, the as-filed specification does not provide sufficient guidance for one skilled in the art how to induce a balanced Th1/Th2 immune response in any host using an immunogenic composition comprising a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment thereof, a promoter sequence operatively coupled to said first nucleotide sequence for expression of said RSV G protein in the host, and a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein in vivo from said vector in any host other than the experimental mice. Thus, it is not apparent how one skilled in the art determines, without undue experimentation, which of the disclosed DNA complexes claimed in the disclosure generate a treatment

(encompasses partial/complete protection) or prevention (total protection) in any nucleic acid therapy methods as contemplated by the as-filed specification, particularly given the unpredictability of nucleic acid therapy as a whole and/or the doubts expressed in the art of record.

Furthermore, with respect to claims encompassing a vector that will not replicate in a mammal the as-filed specification contemplates a vaccine composition comprising a replicant defective vector comprising a first nucleotide sequence encoding a RSV G protein or fragment thereof, a promoter sequence operatively linked to said first nucleotide sequence, a second nucleotide sequence located between said first nucleotide sequence and said promoter sequence to increase expression of said RSV G protein in vivo from said vector. One skilled in the art would determine that a vector that will not replicate in a host could read on a defective viral vector or a plasmid. The disclosure provides sufficient description for one skilled in the art to produce the immunogenic composition comprising replicant defective vector, PXL5 or PXL6, (a **plasmid** encoding a gene encoding a full length membrane attached form of the RSV G protein and containing the CMV intron A sequence or gene encoding a secreted form of the RSV G protein lacking the trans-membrane domain and the CMV intron A sequence as well as a nucleotide sequence encoding a signal peptide of the human tissue plasminogen activator, respectively). The disclosure does not provide sufficient guidance for how to make and/or use any other replicant defective vector [*e.g.* **viral vectors** (adenovirus, adeno-associated virus, and retrovirus)]. In view of the doubts expressed by Anderson and Verma and it would take one skilled in the art an undue amount experimentation to determine what replicant defective viral vector could be used to produce the vaccine composition in the claimed invention.

In addition, to the concerns discussed above, the as-filed specification does not provide sufficient description of a second nucleotide sequence located between first nucleotide sequence and promoter of plasmid vector said to increase expression of said RSV G protein in vivo. The specification is enabled for using the specific combination consisting of a CMV promoter and a second nucleotide sequence encoding a human CMV intron A sequence. However, just because the effect of intron A using human CMV was well known in the art (Applicant's IDS 19, abstract), this knowledge does not provide sufficient guidance for one skilled in the art to reasonably extrapolate to make and/or use any other immunogenic composition in the claimed invention. Because it would require one skilled in the art an undue amount of experimentation to determine what specific combination comprising of any promoter other than the CMV promoter and any nucleotide sequence other than the CMV intron A located between the first nucleotide sequence would increase the expression of said RSV G protein in vivo from said vector in the host. It is not apparent to one skilled if any enhancer, transcription factor, exogenous nucleotide sequence, another promoter, etc. would produce the desired expression of said RSV G protein in vivo. Since each combination (*e.g.* promoter and enhancer) depends on a particular nucleotide sequence to function properly (Voet and Voet, *Biochemistry*, John Wiley and Sons, 1990, pg. 866).

In addition with respect to claims encompassing a method of immunizing against RSV and/or a method of producing a vaccine in any host for treatment (encompasses partial/complete protection) or prevention (total protection) including any host (*e.g.* bird, fish, snake, mammal, etc.) wherein any administration route including injection route is contemplated. The applicants provide sufficient guidance for intramuscular administration of the immunogenic composition in

the 1-4, listed above; however, the as-filed specification does not provide sufficient guidance for any other route of administering the immunogenic composition.

In addition to the doubts expressed in Anderson and Verma, the state of art exemplified by McCluskie et al. (*Molecular Medicine*, 5, pp. 287-300, 1999) teach that "the realization that results in mice often do not predict the situation in humans has also led to a large number of DNA vaccine studies in non-human primates", that "IM injection of plasmid DNA vaccines, while highly immunogenic in mice...was found only to be relatively so in chimpanzees..., and especially not all in Aotus monkeys"' and that "it is probably safe to say that any vaccine that works in a human will work in a mouse, but note necessarily vice-versa" (page 296, column 2, second and third paragraphs). In addition, McCluskie et al. teach that "although non-human primate models are frequently used for development and testing of human vaccines, it is not clear how predicative they will be in the case of DNA vaccines where efficacy, by virtue of the requirement first to transfect cells and express the antigen, relies on many factors other than immunological reponses to the antigen" (page 297, column 1).

Thus, it is not apparent as how one skilled in the art reasonably extrapolates, without undue experimentation, from the scope of vertebrate to the full scope of the claimed invention that would generate a treatment (encompasses partial/complete protection) and/or prevention (total protection) in any subject against any disease. Even if a protective response has been shown in mice using the experimental mice, it is not apparent as to how the mouse model wherein it is reasonably extrapolated to the full scope of the claimed invention, encompassing any host (*e.g.*, snake, bird, fish, mammal, etc.) particularly given that there is no vaccine

generation evidence showing that the mice model is a general phenomenon, and given the doubts expressed in the art of record.

With respect to vaccination methods encompassing routes of administration, e.g., intranasally and intramuscular, the state of the art exemplified by McCluskie teaches that the route of delivery of the DNA vaccine can have an impact on the efficiency of transfection as well as the types and location of cells transfected, and thus potentially on the nature of the immune response (pg. 295). In addition, McCluskie teaches that many different routes have been shown to be effective for DNA delivery in mice; however, few studies have compared responses obtained with different routes using the same antigen-expressing DNA, dose, and immunization schedule. There have been even fewer studies to compare routes of administration in non-human primates (pg. 295).

At best, the application and the state of the art only provide sufficient guidance for enabling claims directed to 1) An immunogenic composition comprising a vector that will not replicate, wherein the vector comprises: a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment, a promoter sequence operatively linked to said first nucleotide sequence for expression of said RSV G protein, a second nucleotide sequence encoding the human cytomegalovirus Intron A; 2) A method of stimulating an immune response in a mammal using an effective amount of the composition of 1; 3) A method comprising isolating gene encoding a RSV G protein or a RSV G fragment, operatively linked said gene to at least one control sequence to produce a vector that will not replicate in mammal; 4) Administering composition of 3 to a mammal, so as to stimulate an immune response in said mammal.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made only provide sufficient guidance and/or evidence to reasonably enable the claimed invention 1-4, listed above. One would have to engage in a large quantity of experimentation in order to practice the claimed invention based on the application's disclosure, the unpredictability of gene therapy (Anderson, *Nature*, Vol. 392, pp.25-30, 1998) and developing effective vaccines (Gurunathan et al., *J Immunol*, Vol. 161(9), pg. 4536, 1998) encompassing any vertebrate subject including any mammal for a protective effect and/or treatment. In addition, the presence of a working example as provided in the specification does not extrapolate to the full scope of the claimed invention, particularly given that there is no evidence that the mice model is a general phenomenon.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 1, 3, 15, 17, 36-38, and 40 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1, 15, and 40 are vague and indefinite in referencing a "second nucleotide sequence" that increases expression of the RSV G protein since the precise structural characteristics of the sequence net set forth. Applicants should clearly and unambiguously identify the structural and functional requirements of said sequence (*e.g.*, wherein said second nucleotide sequence comprises the human cytomegalovirus intron A).

Claims 3 and 17 are vague and indefinite in referencing "said nucleotide sequence comprises the nucleotide sequence shown in Figure 2 (SEQ ID NO: 1)". Applicants should

clearly and unambiguously identify which nucleotide sequence these claims are referring to (*e.g.* first nucleotide sequence or second nucleotide sequence).

Claims 36-38 are vague and indefinite for referencing an "immunoprotection enhancing sequence" since the precise structural and functional characteristics of the sequence are not set forth. Applicants should clearly and unambiguously identify the salient features of the regulatory element.

Some of the following rejections under 102 and/or 103 are directed to the part of the claimed invention that encompasses an immunogenic composition comprising a vector that will not replicate, wherein the vector comprises: a first nucleotide sequence encoding a respiratory syncytial virus (RSV) G protein or a RSV G protein fragment, a promoter sequence operatively linked to said first nucleotide sequence for expression of said RSV G protein, a second nucleotide sequence. Since, it is not apparent what the applicants are claiming (*e.g.* 112 2nd against claims 1 and 15 and 112 1st written description) **as the second nucleotide sequence located between the first nucleotide sequence and promoter to increase expression of RSV G protein. Any prior art displaying a second nucleotide sequence displaying the characteristics listed above is readable on the claimed invention.**

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-2, 6, 15, 16, 24, 26, 30-35, 40 and 42 are rejected under 35 U.S.C. 102(b) as being anticipated over Schrijver et al., (*Vaccine*, Vol. 16, pp. 130-134, 1998). Schrijver teaches construction of an immunogenic composition comprising a plasmid with the eukaryotic expression vector pVR1012 comprising a synthetic gene that codes for the G protein of BRSV with a human CMV promoter followed by a second nucleotide sequence (5' UT) located between the promoter and RSV G protein (page 131, and page 131, Figure 1). Furthermore, Schrijver uses the immunogenic composition to prime the immune response of the respiratory mucosa in cattle (abstract).

Claims 30-35 are rejected under 35 U.S.C. 102(b) as being anticipated by Stott et al., (*Journal of Virology*, Vol. 60, pp. 607-613, 1986). Stott displays that RSV G protein expressed from a recombinant vector (plasmid) protects mice against a live virus challenge (abstract). Sttot produced a plasmid containing a complete cDNA copy of the G gene (page 607). Stott teaches that the G protein expressed from the recombinant vector induced antibodies in rabbits (page 607).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a), which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or non-obviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-2, 4-7, 10-12, 15-16, 18-21, 24-26, 30-38, 40, 42 are rejected under 35 U.S.C. 103(a) as being unpatentable over Schrijver et al., (*Vaccine*, Vol. 16, pp. 130-134, 1998) in further view of Garcia et al., (*Journal of Virology*, Vol. 68, pp. 5448-59, 1994). Schrijver teaches construction of an immunogenic composition comprising a plasmid with the eukaryotic expression vector pVR1012 comprising a synthetic gene that codes for the G protein of BRSV (page 131 and page 131, Figure 1). Furthermore, Schrijver uses the immunogenic composition to prime the immune response of the respiratory mucosa in cattle (abstract). However, Schrijver does not teach the construction of an immunogenic composition comprising of a nucleotide

sequence encoding a full length RSV G protein having the amino acid sequence shown in applicant's application, Figure 2 (SEQ ID NO: 2).

However, at the time the invention was made, Garcia reports the genetic and antigenic variability of the G glycoproteins from 76 human syncytial virus (RSV) isolated during epidemics in several countries (abstract). In Garcia's analysis, he identifies a full-length RSV G amino acid sequence that is 100% identical (result 1) to applicants' sequence (SEQ ID NO: 2).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Schrijver taken with Garcia, namely to produce an immunogenic composition comprising any sequence from Garcia's analysis (including SEQ ID NO: 2 from applicant's application). One of ordinary skill in the art would have been motivated to use the nucleotide sequence encoding amino acid sequence SEQ ID NO: 2 in an immunogenic composition to produce an immune response against RSV as taught by Schrijver.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 1-12, 15-26, 30-38, 40, 42 are rejected under 35 U.S.C 103(a) as being patentable over Schrijver taken with Garcia in further view of Klein (WO 93/14207).

The rejections of the base claim 1-2, 4-7, 10-12, 15-16, 18-21, 24-26, 30-38, 40, 42 under 35 U.S.C. 103(a) are applied here as indicated above. Schrijver and Garcia do not teach an immunogenic composition comprising a truncated RSV G protein encoding SEQ ID NO: 3 or SEQ ID NO: 4 (applicants' application, Figure 3).

However, at the time the invention was made, Klein teaches a multimeric hybrid gene, comprising a gene sequence coding for an antigenic region of a protein from a first pathogen linked to a gene sequence coding for an antigenic region of a protein from a second pathogen, wherein the hybrid gene consisting for a human PIV-3 F or Hn protein or an immunogenic epitope-containing fragment thereof linked to a gene sequence coding for a human RSV G protein or F protein or an immunogenic epitope-containing fragment thereof (page 36-37 claim 11, Figure 7A-7D). The sequences (Figure 7A-7D) listed in WO document are 100% identical to Figure 3 in applicants' application.

It would have been *prima facie* obvious for a person of ordinary skill in the art at the time the invention was made to combine the teaching of Schrijver and Garcia taken with Klein to produce an immunogenic composition comprising RSV G protein encoding SEQ ID NO: 3 or 4 to produce an immune response in a mammal. One of ordinary skill in the art would have been motivated to employ the immunogenic composition encoding either a nucleotide sequence encoding either SEQ ID: 3 or 4 to prime an immune response in a mammal, as taught by Schrijver.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Claims 15-28 and 30-39 are rejected under 35 U.S.C. 103(a) as being unpatentable over Roberts et al. (Applicants' IDS 31) in further view of Herrmann et al (Applicants' IDS, US patent 5,620,896, 1997). Roberts provides the completed nucleotide sequence of the RSV G protein (abstract). However, Roberts does not employ the nucleotide sequence of the RSV G protein in a method of stimulating an immune response in a host against RSV. Furthermore,

Roberts does not teach a method of using a gene encoding RSV G protein fragment that generates antibodies that specifically react with RSV G protein, to produce an immune response in a host, which comprises isolating said gene, operatively linked said gene to at least one control sequence to produce a vector that will not replicate when introduced into the host, said control sequence directing expression of said RSV G protein when introduced into a host to produce an immune response to said RSV G protein and introducing said vector into host.

However, at the time the application was filed, Herrmann provides a control plasmid pCMVIA, a bacterial plasmid that includes SV40 replication origin, the CMV promoter, Intron A and a bovine growth hormone gene that provides a polyadenylation signal. (column 5, lines 56-63). Furthermore, Herrmann uses the plasmid, wherein the promoter is operably linked to a nucleotide sequence encoding a rotavirus polypeptide wherein said rotavirus polypeptide is expressed in a cell of a mammal with said plasmid vector (column 27, lines 39-45).

It would have been *prima facie* obvious for a person of ordinary skill in the art at the time the invention was made to combine the teaching of Roberts and Herrmann to produce an immunogenic composition comprising a RSV G protein to produce an immune response in a mammal. One of ordinary skill in the art would have been motivated to produce this composition since it would facilitate the expression of large quantities of the immunogen for future research purposes.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ms. Tracey Johnson whose telephone number is (703) 305-2982.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775. The examiner can normally be reached on M-F, (730-400 EST).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah Clark can be reached at (703) 305-4051.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 746-5024.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1633
July 30, 2001

DAVE T. NGUYEN
PRIMARY EXAMINER